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KATCHERES, K	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/607,361	SHIGEMORI ET AL.	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☒ Other: *Notice to comply* .

DETAILED ACTION

Claims 1-22 are pending in the instant application.

Information Disclosure Statement

Applicant should note that Applicant omitted figure 2 and several of the claims of Ferrin et al., WO 97/04111, when the IDS was submitted.

Specification

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Figures 1 and 2 contain sequences which fail to recite the appropriate sequence identifiers. Furthermore, it is not immediately apparent that these sequences in the figures are all listed in the sequence listing provided by applicant. According to 37 CFR 1.821 through 1.825, Applicants are required to assign a sequence identifier (SEQ ID NO) for every

disclosed unbranched nucleic acid sequence of 10 or more nucleotides and list these sequences individually in a Sequence Listing as a separate part of the disclosure.

For the purposes of compact prosecution Applicant is given three months to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). A complete response to this Office Action requires that Applicants comply with the sequence rules, and that pending rejections be addressed. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Figures

Pages 4 and 5 of the specification contain the descriptions of the drawings. The explanations for Figures 7, 8 and 9 are incomplete. The figures should be completely described. The instant figures are incomplete because they do not refer to each of the figures associated with that figure number. For example, figure 7 in the specification should also properly identify figures 7(a) and 7(b).

Objections

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are:

1) The sentences on page 2, line 35 and page 5, line 15 are verbose and unclear. A double-stranded end of a DNA is by definition a double-stranded end of a DNA. The attempts in the disclosure to define terms and limitations simply by repeating the term or limitation is inherently unclear and does not elucidate the scope of Applicant's invention.

2) Pages 6, 8 and 11 contain sentences which parenthetically contain other sentences within them. Such sentence structure confuses a reader and makes the point of the sentence unclear.

3) Page 1, line 17 contains a wordy verbose sentence that alone makes up an entire paragraph. The sentence further contains the unnecessary transitional word "as-it-is."

4) The specification contains several grammatical errors. For example, the sentence on page 11, line 9 contains an improper verb tense. The sentence on page 11, 20 says PCT when it should say PCR. The term three-stranded on page 12, line 12 is misspelled. Applicant uses the term "DNA constitute" when it appears that Applicant more likely intends to use the term "DNA constituent."

5) The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. New application papers with lines double spaced on good quality paper are required.

The above examples merely represent the errors in the specification. They are not meant to be all-inclusive. Applicant should be cognizant when making any corrections that there may be other errors encompassed by the explanations to the examples above.

Appropriate correction is required.

Claims 2 and 21 are objected to because of the following informalities: Claim 2, line 2 has the word complex misspelled and claim 21 contains the wrong verb tense. Additonally, some claims recite RecA spelled "RecA" and others recite it spelled "Rec A." Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Statutory Type Double Patenting

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 respectively of co-pending Application No. 09/549,949. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The conflicting claims provisionally rejected are not verbatim, yet the scope of the inventions are identical. The instant claims merely include superfluous and additional language that does not alter the scope of the invention claimed such that they are patentably distinct inventions. Absent the superfluous language within the claims, the claims of the patent and the instant claims are identical.

The above claim is rejected as double patenting.

Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. 09/549,949 in view of Ferrin et al. Although the conflicting claims are not identical, they are not patentably distinct from each other.

It would have been obvious to one of skill in the art to use the single-stranded DNA on the ends of the double-stranded DNA as elements of the triplex claimed in the application cited for the cleavage of the dsDNA. In light of the claims of Application No. 09/549,949, it would have been obvious to one of skill in the art that the ssDNAs form a triplex with the dsDNA such that cleavage occurs selectively within or adjacent to the region of triplex formation. Said triplex comprises a dsDNA, a single-stranded sequence with sufficient homology with the dsDNA formed by RecA, or a RecA like protein, in the presence of a nucleoside triphosphate or an analogue thereof. The claims of the application cited encompass any single-stranded DNA for the practice of the invention, and thus the instant invention. Additionally, the claims recite a limitation wherein RecA three stranded complexes flank a double-stranded DNA sequence. Since it is an element of the invention that a double-stranded DNA sequence have two single-stranded end, it would be an obvious extention of the teachings in the Application to form the RecA three stranded complexes where there are single strands, i.e. have flanking RecA three stranded complexes. Therefore, the instant claims are an obvious and logical extension and variation of the invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11 and 13-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Ferrin et al. (WO 97/04111).

Applicant's invention comprises a method and composition for the nuclease cleavage of a double-stranded DNA (dsDNA). Said cleavage occurs selectively within or adjacent to a region of triplex formation. The triplex comprises the dsDNA and single-stranded DNA (ssDNA) from the ends of the dsDNA with sufficient homologous sequences with the dsDNA for undergoing recombination, whereby a homologous recombinant protein forms said triplex in the presence of a nucleoside triphosphate or an analogue thereof. The triplex claimed by Applicant flanks said dsDNA.

Ferrin et al. discloses a method of RecA assisted gene-cloning. Ferrin et al. discloses a method comprising RecA protein and oligonucleotides complementary to a genomic dsDNA of interest such that a resultant three-stranded complex is formed. The three stranded complex flanks a gene of interest so that protected fragments flanked by the triplex structures are selectively cloned. See pages 3, lines 15-21, page 5 and page 7. Ferrin et al. further discloses that the sequence thus flanked by the Rec A three stranded complexes is inserted into a vector and then into a cell. The concept of RecA mediated selective ligation is also utilized by Ferrin et al. to selectively clone certain DNAs of interest. Applicant's invention

comprises triplex structures flanking dsDNA that may encode a gene of interest that is ultimately inserted into a vector. Applicant's invention encompasses the same scope as the method taught in Ferrin et al. wherein a triple-stranded DNA complex with RecA is used for the selective ligation and cloning of the dsDNA.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the

time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al. (J. of Bio. Chem. Vol. 256, issue 4 1981) in view of Camerini-Otero et al. (A) (Annu. Rev. Gen. Vol. 29 1995) and Camerini-Otero et al. (B) (US Patent 5,460,941).

Applicant's invention comprises a method for the nuclease cleavage of double-stranded DNA. Said cleavage occurs selectively within or adjacent to a region of triplex formation. The triplex comprises the dsDNA and a single-stranded DNA with sufficient homologous sequences with the dsDNA for undergoing recombination, whereby a homologous recombinant protein forms said triplex in the presence of a nucleoside triphosphate or an analogue thereof.

Williams et al. teaches the enhancement of stability of dsDNA against nuclease degradation comprising the addition of a homologous recombination protein and nucleoside triphosphate to the dsDNA. See pages 7573 and7574. However, Williams et al. does not teach the selective nuclease cleavage of dsDNA in the region of homologously combining ssDNA with dsDNA and further comprising the formation of the triplex in the presence of a homologous recombinant protein and a nucleoside triphosphate or analogue thereof.

Camerini-Otero et al. (A) teaches the inhibition of random nuclease degradation by non-specific nucleases and also teaches the selective nuclease cleavage of dsDNA by the non-specific nuclease at the site of triplex formation in the presence of a homologous recombinant protein and a nucleoside triphosphate or analogue thereof. See page 513 and 518. Camerini-Otero et al. (A), however, fails to specifically teach RecA.

Camerini-Otero et al. (B) specifically teaches RecA in the characterization of dsDNA by comparing nuclease susceptibility in the presence and absence of RecA protein (column 11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a homologous recombinant protein such as RecA to coat a dsDNA molecule to protect it from non-specific nuclease degradation. Williams et al. had previously taught this function. Through the teachings of Camarini-Otero et al. (A), it was also known to those of ordinary skill in the art that the non-specific nuclease RecBCD selectively cleaves target dsDNA within the region of triplex formation with homologous ssDNA in the presence of homologous recombinant protein RecA and nucleoside triphosphate. One of ordinary skill in the art would have been motivated to selectively cleave target dsDNA using appropriately homologous ssDNA for triplex formation with the desired target dsDNA sequences in combination with a non-specific nuclease, a homologous recombination protein and a nucleoside triphosphate. This technique had been known in the art and the selective fragmentation of large spans of DNA is obtained in this manner for purposes including further characterization and cloning.

Claims 12, 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrin et al.

Various elements of Applicant's invention are described above. As discussed above Ferrin et al. discloses all the elements of Applicant's invention except for the limitation that the desired DNA constituent is inserted into cells via electroporation of claim 12 and the gene cloning kit of claims 21-22. With respect to electroporation, it would have been obvious to

one of ordinary skill in the art at the time the invention was made to use electroporation to insert the desired DNA constituent into a target cell. Electroporation is a well-known method in the art for transporting material into cells by applying an electric field to the cells such that the cell membrane contains transient pores. One of ordinary skill in the art would be motivated to use electroporation because it is such a well-known method and effective method for the transport of varied compounds and materials across a cell membrane.

With respect to the gene cloning kit, the ordinary skilled artisan would have been motivated to apply the method taught and disclosed in Ferrin et al. to create a kit. The ordinary skilled artisan would have been motivated to create a kit with said method for the purposes of efficiency and commercial marketability. Therefor, it would have been obvious to one skilled in the art to take the teachings of Ferrin et al. and create the kit recited in Applicant's claims 20-22.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant should note that the following claim rejections are meant to be as thorough and precise as possible. However, the claims are verbose and replete with errors such that

some rejections pursuant to 35 U.S.C. 112, second paragraph may have been overlooked. Applicant should keep this in mind when amending any claims.

The following claims fail to particularly point and distinctly claim Applicant's invention:

Claims 1 and 2 contain circular language rendering them difficult to understand. The claims recite the single-stranded region end of a double-stranded DNA having a single-stranded region end. By definition a fragment of dsDNA with a single-stranded end will have a single-stranded end. Likewise, double-stranded DNA by definition has double-stranded end. Such superfluous and unnecessary language has the effect of rendering the instant claims difficult to understand or altogether unintelligible.

Claim 1 contains the phrase "contacting, under the presence of[.]" The word, under, connotes location as used. The claim as written does not make it explicitly clear what is contacted; the single-stranded DNA, the double-stranded DNA, the homologous recombinant protein, all of them or some of them. In short, the actual limitations that are intended are unclear.

Throughout claims 1-22, Applicant often refers to double-stranded regions, double-stranded region end, double-stranded DNA, double-stranded nucleotide region and double-stranded DNA segment. Applicant also refers to single-stranded regions, single-stranded region end, and single-stranded DNA. It is often, unclear whether all these terms refer to the same aspects of Applicant's invention or are entirely different. Lack of clarity in the use of terms makes the metes and bound of the invention virtually impossible to determine.

Throughout claims 1-19, Applicant uses the terms "three-stranded structure" and "three-stranded structural portions." It appears that these terms may describe the same triplex. However, they can reasonably be interpreted to relate to different three-stranded structures as well. For the purposes of clarity, the inconsistencies within the claims must be resolved.

Claims 5 recites the limitation "one DNA." In light of the preceding claims from which claim 5 depends, it is not immediately apparent which DNA Applicant is referring. Does Applicant mean all of the DNA's described, one specific DNA described or a completely different DNA. Claim 5 is thus unclear and renders Applicant's invention vague and indefinite.

Claims 5, 20 and 21 recite the phrase "capable of" which renders the claims indefinite because the capacity of a compound to perform some function is merely a latent characteristic of said compound. The language implies a mere possibility of function is sufficient such that it is not apparent whether Applicant actually intends said function to be a limitation.

Claim 9 is vague and indefinite as to the metes and bounds of the claim because they claim a "nucleoside triphosphate or a derivative thereof [emphasis added]." "Derived" is a term that is non-specific and relative in nature for which Applicant provides no definition. It provides no clarity as to what Applicant's claimed invention includes and what it does not include. Without a more specific definition of the claim, it is impossible to determine what and how many derivations comprise the invention. Applicant's disclosure does not provide any definition as to the process of deriving the nucleoside triphosphates encompassed by the

claims nor what is included in the definition of a "nucleoside triphosphate or a derivative thereof."

The nature and number of the derivations to arrive at the invention Applicant seeks to protect with the patent are not established such that a person skilled in the art may replicate the invention without undue experimentation. The limits of the inventions cannot be discerned and others could not possibly know if they were infringing Applicant's claim. Thus, the imprecision of the claim as written makes the metes and bounds of the invention unclear such that the instant claims are rejected pursuant to 35 U.S.C. 112, second paragraph.

Claim 19 recites that a double-stranded DNA is "sandwiched" between three-stranded structural portions. Where is the double-stranded DNA? Do the three-stranded structural portions linearly flank the double-stranded DNA of the claim or are they positioned above and below the double-stranded DNA? The actual positions of the elements recited in the claim are inherently unclear rendering the claims vague and indefinite.

The term "different" in claim 21 is a relative term which renders the claim indefinite. The term "different" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Neither claims nor the specification disclose how different the sequences are from each other rendering the claim vague and indefinite.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves, J.D. whose telephone number is (703) 305-1999. The examiner can normally be reached on Monday through Friday 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richard Schwartz, Ph.D. can be reached on (703) 308-1133. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3388.

Konstantina Katcheves
February 9, 2001

REMY YUCEL, PH.D
PRIMARY EXAMINER